REMARKS

The Examiner is thanked for reconsidering and withdrawing the restriction requirement.

Claims 6, 11, 13 and 15 were rejected under 35 U.S.C.§112, first paragraph as not being enabling with regard to the prevention of the constipating effect of oxycodone with naloxone.

Reconsideration is requested.

The Examiner contends that the information given in the specification is inadequate to allow the skilled artisan to practice the invention without undue experimentation. The Examiner has not stated how much experimentation would be "undue" and it must be conceded that at least some experimentation is allowed without leading to a conclusion that a particular method is not enabled.

The instant rejection is based on a statute that requires an applicant for a patent to provide sufficient information that would enable one skilled in the art to make and use the invention. No issue has been raised with regard to the detailed information as to how to make the product of the invention. The information as to how to use the product is implicit in the disclosure where the dosages are described at page 7, lines 33-40 in functional terms that are readily understood and determined by those who are skilled in the pharmacological art. Thus, there can be no serious question regarding the fact that the applicant has taught the art how to make and use the invention.

The thrust of the Examiner's arguments appear to be that the specification does not provide any teachings that show that administration of the product of claims 6, 11, 13 and 15 would prevent the constipating effect of oxycodone due to the

coadministration of naloxoxne. This rejection appears to be in effect based on the premise that the invention is inoperative rather than not enabled. The method of making the formulations of the Examples are detailed and the doses are readily derived from the Examples and the specification.

MPEP§2107.01 (Rev. 1, Feb 2003) discusses at length the relation between Section 101 and Section 112, first paragraph. All that is required by 35 U.S.C.§101 is that some use for the claimed invention must be set forth in the specification. This has been done in the present specification. The requirements of 35 U.S.C.§112, first paragraph may only be properly used to reject patent claims if one skilled in the art could not practice the claimed invention based on the disclosure. The Examiner has urged that an unreasonable amount of experimentation would be required for one to make and/or use the claimed invention. Attention is directed to MPEP§2164.01(c) (Rev. 1, Feb 2003) which points out that "if a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C.§112 is satisfied. In the present case, it is apparent that this standard has been met.

In virtually every patent for a new pharmaceutical, the disclosure regarding utility merely states a condition, a host, a dose and sometimes a route of administration for the new chemical compound. There are typically no reports of clinical studies, toxicology, stability, side effects, drug interactions etc. which are required by the FDA as a basis for the approval of the sale of the new chemical compound for use in humans. The courts have repeatedly instructed the PTO that human clinical data is not required to establish utility. Cf. MPEP§2107.03 If human clinical data is unnecessary to establish utility, it is not seen how such data would be necessary to satisfy the "how to make and use" standard of 35 U.S.C.§112, first paragraph.

The province of drug safety and efficacy belongs to the FDA and not to the PTO. See *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995) and MPEP§2107.01 (Rev. 1, Feb 2003)

The Examiner has cited the decision in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) in support of the present rejection. The Wands decision listed eight factors to be considered in connection the question of enablement: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the art, and (8) the breadth of the claims. With regard to factor (1) it is submitted that there is little or no experimentation to provide the composition of the invention to one who is suffering from a painful condition according to the specification. Factor (2) relates to the amount of direction or guidance. As noted previously, the invention is practiced by determining if pain requires the administration of an analgetic to a host who has pain. The concern of factor (3) does not arise, because it is not necessary for the specification to recite that which is already known, i.e how to administer an solid oral dosage form. The nature of the invention (Factor 4) does not cause undue experimentation because the invention involves pain treatment by using an opiate based formulation that is not susceptible of easily being converted to and injectable formulation with enhanced potential for abuse. The improved result of reducing or eliminating constipation is not based on a specific technique of administration as it is based on the use of the fully disclosed composition that is illustrated by the Examples.

The state of the art (Factor 5) does not provide any basis on which to urge that undue experimentation is required to practice the invention. The Examiner has cited McNichol et al., J. of Pain. V.4, No. 5 (2003) pp231-256 as disclosing

that naloxone has been given to patients taking opiates for pain. However, this reference is concerned with uncoated oral naloxone which can antagonize the analgetic effect of the opiate while the formulations of amended claim 6 are enteric coated pellets of naloxone which do not release in the stomach and are readily distinguishable from the uncoated immediate release McNichol formulations. Factor 6, is related to the level of skill in the art. This invention is related to pain treatment and the avoidance of the abuse of controlled substances. The level of skill is quite high with virtually all those in the art having one or more postgraduate degrees with many years of practical experience. Factor 7 relates to predictability in the art which does exist in the present application. If simple tests are carried out on a small group of patients, it would be reasonable to extrapolate those results to other patients thus avoiding the prohibition of the somewhat ephemeral concept of "undue experimentation" to determine optimum dosing and timing of administration. Wands mentions the concept of undue experimentation but does not quantify what actually does constitute undue experimentation. The inventor has disclosed in the present application that the combination of the hydrocolloid and an opiate with an opiate antagonist has been It should be noted that the mention of predictability in connection with the first paragraph of 35 U.S.C.§112, has to do with the "make" requirement where consideration may be given to uncertainty or chance which arises when one tries to make a new material. It does not relate to the operability or usefulness of an invention which is an admitted fact in the present application because of the absence of any rejection under 35 U.S.C.§101 that is directed to operability.

The breadth of the claims is a Wands factor (Factor 8) that does not arise in the present application because the amended claims are specific to the use of named materials. in an identified host (newborns and infants). If there is no issue as to operability, there can be no issue of undue breadth in the present application because the claims specify the use of particular materials which are readily available from commercial sources.

The Examiner has not cited any missing information regarding the "how to make and use" requirements of U.S.C.§112, first paragraph. The question of the operability of the claimed method is not properly raised under 35 U.S.C.§112, first paragraph unless reasons can be given that are directed to the lack of information as to how to carry out the invention.

In order to show usefulness, it is not necessary to show statistically significant data relating to the alleged use. *Nelson v. Bowler*, 206 USPQ 881,883 (CCPA 1980). If it is not necessary to show statistically significant data to show usefulness, statistically significant data should not be required for the purpose of showing compliance with 35 U.S.C.§112, first paragraph. For these reason, it is requested that this ground of rejection be withdrawn.

Claims 1-11 and 19-20 were rejected under 35 U.S.C.§102(e) as anticipated by Oshlack et al. (Oshlack).Claims 12-15 were rejected under 35 U.S.C.§103(a) as being unpatentable over Oshlack.

Reconsideration is requested in view of this Amendment.

Claim 1 has been amended to recite specific hydrocolloids and excipients as disclosed in the specification in Examples 1 and 2. This specific

formulation is not disclosed or make obvious by Oshlack who mentions many formulations but none having the hydrocolloid components of claim 1.Claim 6 recite the formulation of enteric coated pellets for reducing or eliminating constipation. This formulation is not made obvious by Oshlack. Claim 16 points out a specific three pellet formulation where the pellets are formulated to release the drugs in specific anatomical locations of the small intestine. This formulation is not anticipated or made obvious by Oshlack. New claim 22 points out a method of reducing constipation caused by opiates by the administration of the opiate antagonist in the form of particular enteric coated pellets. For these reasons, it is requested that this rejectionds over Oshlack be withdrawn.

An early and favorable action is earnestly solicited.

Respectfully submitted,

James V. Costigan
Reg. No. 25,669

Hedman & Costigan, P.C.
1185 Avenue of the Americas
New York, NY 10036
(212) 302-8989